

WHAT IS CLAIMED IS:

1 1. A method for identifying a monomer domain that binds to a target
2 molecule, the method comprising,
3 providing a library of monomer domains, wherein the monomer domains each
4 bind an ion;
5 screening the library of monomer domains for affinity to a first target
6 molecule; and
7 identifying at least one monomer domain that binds to at least one target
8 molecule.

1 2. The method of claim 1, wherein the ion is selected from calcium or
2 zinc.

1 3. The method of claim 1, wherein the monomer domain is selected from
2 the group consisting of an A domain, EGF domain, EF Hand, Cadherin domain, C-type
3 lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and zinc finger.

1 4. The method of claim 1, further comprising linking the identified
2 monomer domains to a second monomer domain to form a library of multimers, each
3 multimer comprising at least two monomer domains;
4 screening the library of multimers for the ability to bind to the first target
5 molecule; and
6 identifying a multimer that binds to the first target molecule.

1 5. The method of claim 1, wherein the monomer domains are between 25
2 and 500 amino acids.

1 6. The method of claim 1, wherein each monomer domain of the selected
2 multimer binds to the same target molecule.

1 7. The method of claim 1, wherein the selected multimer comprises at
2 least three monomer domains.

1 8. The method of claim 1, wherein the selected multimer comprises four
2 monomer domains.

1 9. The method of claim 4, comprising identifying a multimer with an
2 improved avidity for the target compared to the avidity of a monomer domain alone.

1 10. The method of claim 1, wherein the monomer domain is an LDL
2 receptor class A domain monomer comprising the following sequence:

3 $C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$

4 wherein C is cysteine, X_{n-m} represents between n and m number of
5 independently selected amino acids, and (D,N) indicates that the position can be either D or
6 N; and

7 wherein C_a-C_c , C_b-C_e and C_d-C_f form disulfide bonds.

1 11. The method of claim 10, wherein the monomer domain is an LDL
2 receptor class A domain monomer comprising the following sequence:

3 $CaX_{6-7}CbX_{4-5}CcX_6CdX_5CeX_{8-10}Cf$

4 wherein X is defined as follows:

X(6,7)							X(4,5)				X(6)						X(5)					X(8,10)							
X1	X2	X3	X4	X5	X6		X1	X2	X3	X4	X1	X2	X3	X4	X5	X6	X1	X2	X3	X4	X5	X1	X2	X3	X4	X5	X6	X7	X8
A	A	A	A	A	A		A	A			A	A	A	A	A		A	A	A			A	A	A			A	A	
D	D	D	D				D	D	D	D	D	D	D	D	D		D	D	D	D	D	D	D	D	D	D	D	D	D
E	E	E	E		E		E	E	E	E	E	E	E	E	E		E	E	E	E	E	E	E	E	E	E	E	E	E
F	F	F	F	F	F		F	F	F	F	F	F	F	F	F		F	F	F	F	F	F	F	F	F	F	F	F	F
G	G	G	G	G	G		G	G	G	G	G	G	G	G	G		G	G	G	G	G	G	G	G	G	G	G	G	G
H	H	H	H	H	H		H	H	H	H	H	H	H	H	H		H	H	H	H	H	H	H	H	H	H	H	H	H
I	I	I	I	I	I		I	I	I	I	I	I	I	I	I		I	I	I	I	I	I	I	I	I	I	I	I	I
K	K	K	K	K	K		K		K	K	K	K	K	K	K		K	K	K	K	K	K	K	K	K	K	K	K	K
L	L	L	L	L	L		L		L	L	L	L	L	L	L		L	L	L	L	L	L	L	L	L	L	L	L	L
M	M			M	M						M	M	M	M	M		M	M				M	M	M	M	M	M	M	M
N	N	N	N	N	N		N	N	N	N	N	N	N	N	N		N	N	N	N	N	N	N	N	N	N	N	N	N
P	P	P	P	P	P		P				P	P	P	P	P		P	P	P	P	P	P	P	P	P	P	P	P	P
Q	Q	Q	Q	Q	Q		Q	Q	Q	Q	Q	Q	Q	Q	Q		Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q
R	R	R	R	R	R		R	R	R	R	R	R	R	R	R		R	R	R	R	R	R	R	R	R	R	R	R	R
S	S	S	S	S	S		S	S	S	S	S	S	S	S	S		S	S	S	S	S	S	S	S	S	S	S	S	S
T	T	T	T	T	T		T	T	T	T	T	T	T	T	T		T	T	T	T	T	T	T	T	T	T	T	T	T
V	V	V	V	V	V		V	V			V	V	V	V	V		V	V	V	V	V	V	V	V	V	V	V	V	V
W	W	W	W	W	W		W	W	W	W	W	W	W	W	W		W	W	W	W	W	W	W	W	W	W	W	W	W
Y	Y	Y	Y	Y	Y		Y	Y			Y	Y	Y	Y	Y		Y	Y				Y	Y	Y	Y	Y	Y	Y	Y

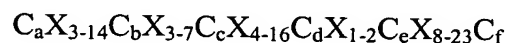
X1	X2	X3	X4	X5	X6	X7
A	A					A
D	D	D	D	D		
E	E	E	E	E		E
F	F	F	F	F		F
G	G	G	G	G		G
H	H					H
K		K	K	K		K
L	L	L		L		L
M			M			M
N	N	N	N	N		
P	P	P	P	P		
Q	Q	Q	Q	Q		
R	R	R	R	R		
S	S	S	S	S		
T	T	T	T	T		
V						V
W						W
Y						Y

X1	X2	X3	X4	X5
A	A	A	A	A
D	D	D	D	D
E	E	E	E	E
F	F	F	F	F
G	G	G	G	G
H	H	H	H	H
I	I	I	I	I
K	K	K	K	K
L	L	L	L	L
M	M	M	M	M
N	N	N	N	N
P	P	P	P	P
Q	Q	Q	Q	Q
R	R	R	R	R
S	S	S	S	S
T	T	T	T	T
V	V	V	V	V
W	W	W	W	W
Y	Y	Y	Y	Y

X1	X2	X3	X4	X5	X6	X7	X8	X9
A	A					A	A	A
D	D			D			D	D
E	E			E	E	E	E	E
F	F			F				
G		G				G	G	
H		H				H		H
L						L		L
M						M		M
N						N		N
P						P		P
Q		Q				Q		Q
R		R				R		R
S		S				S		S
T		T				T		T
V								V
Y		Y						Y

X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
		A				A	A	A	A
D	D			D			D	D	D
E	E			E	E	E	E	E	E
F	F			F					
G		G				G		G	
H		H				H		H	
I		I				I		I	
K		K				K		K	
L		L				L		L	
M						M		M	
N	N					N		N	
P	P					P		P	
Q		Q				Q		Q	
R		R				R		R	
S	S	S				S		S	
T		T				T		T	
V								V	
W						W			
Y						Y			Y

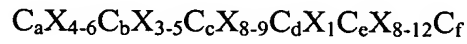
12. The method of claim 1, wherein the monomer domain is an EGF domain monomer comprising the following sequence:



wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids; and

wherein C_a - C_c , C_b - C_e and C_d - C_f form disulfide bonds.

13. The method of claim 10, wherein the monomer domain is an EGF domain monomer comprising the following sequence:



wherein X is defined as follows:

X(4,6)				X(3,5)			X(8,9)								X(1)		X(8,12)							
X1	X2	X3	X4	X1	X2	X3	X1	X2	X3	X4	X5	X6	X7	X8	X1	X1	X1	X2	X3	X4	X5	X6	X7	X8
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
D	D	D	E	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D
E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E
F	F	F	G	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G
H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
K	K	K	L	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K
L	L	L	M	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L
M	M	M	N	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
P	P	P	Q	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Q	Q	Q	R	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q
R	R	R	S	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
S	S	S	T	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
T	T	T	V	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T
V	V	V	W	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V
W	W	W	Y	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
Y	Y	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

14. The method of claim 1, further comprising a step of mutating at least one monomer domain, thereby providing a library comprising mutated monomer domains.

- 1 15. The method of claim 14, wherein the mutating step comprises
2 recombining a plurality of polynucleotide fragments of at least one polynucleotide encoding a
3 polypeptide domain.
- 1 16. The method of claim 14, wherein the mutating step comprises directed
2 evolution.
- 1 17. The method of claim 14, wherein the mutating step comprises site-
2 directed mutagenesis.
- 1 18. The method of claim 1, further comprising,
2 screening the library of monomer domains for affinity to a second target
3 molecule;
4 identifying a monomer domain that binds to a second target molecule;
5 linking at least one monomer domain with affinity for the first target molecule
6 with at least one monomer domain with affinity for the second target molecule, thereby
7 forming a multimer with affinity for the first and the second target molecule.
- 1 19. The method of claim 1, wherein the target molecule is selected from
2 the group consisting of a viral antigen, a bacterial antigen, a fungal antigen, an enzyme, an
3 enzyme substrate, a cell surface protein, an enzyme inhibitor, a reporter molecule, and a
4 receptor.
- 1 20. The method of claim 1, wherein the library of monomer domains is
2 expressed as a phage display, ribosome display or cell surface display.
- 1 21. The method of claim 1, wherein the library of monomer domains is
2 presented on a microarray.
- 1 22. The method of claim 1, wherein the monomer domains form a
2 secondary structure by the formation of disulfide bonds.
- 1 23. The method of claim 1, wherein the monomer domains are linked by a
2 polypeptide linker.
- 1 24. The method of claim 23, wherein the polypeptide linker is a linker
2 naturally-associated with the monomer domain.

1 25. The method of claim 23, wherein the polypeptide linker is a variant of
2 a linker naturally-associated with the monomer domain.

1 26. The method of claim 23, wherein the linker is between 1-20 amino
2 acids.

1 27. The method of claim 23, wherein the linker comprises the following
2 sequence, A₁A₂A₃A₄A₅A₆, wherein

3 A₁ is selected from the amino acids A, P, T, Q, E and K;

4 A₂ and A₃ are any amino acid except C, F, Y, W, or M;

5 A₄ is selected from the amino acids S, G and R;

6 A₅ is selected from the amino acids H, P, and R

7 A₆ is the amino acid, T.

1 28. A method of producing a polypeptide comprising the monomer domain
2 identified in claim 1.

1 29. The method of claim 28, wherein the polypeptide is produced by
2 recombinant gene expression.

1 30. A polypeptide comprising the monomer domain identified in claim 1.

1 31. A polynucleotide encoding the monomer domain identified in claim 1.

1 32. A method for identifying a multimer that binds to at least one target
2 molecule, the method comprising:

3 providing a library of multimers, wherein each multimer comprises at least
4 two monomer domains and each monomer domain exhibits a binding specificity for a target
5 molecule; and

6 screening the library of multimers for target molecule-binding multimers.

1 33. The method of claim 32, further comprising identifying target
2 molecule-binding multimers having an avidity for the target molecule that is greater than the
3 avidity of a single monomer domain for the target molecule.

1 34. The method of claim 32, wherein one or more of the multimers
2 comprises a monomer domain that specifically binds to a second target molecule.

1 35. A method of producing a polypeptide comprising the multimer
2 identified in claim 32.

1 36. The method of claim 35, wherein the polypeptide is produced by
2 recombinant gene expression.

1 37. A method for identifying a multimer that binds to a target molecule,
2 the method comprising,
3 providing a library of monomer domains and/or immuno domains;
4 screening the library of monomer domains and/or immuno domain for affinity
5 to a first target molecule; and
6 identifying at least one monomer domain and/or immuno domain that binds to
7 at least one target molecule;
8 linking the identified monomer domain and/or immuno domain to a library of
9 monomer domains and/or immuno domains to form a library of multimers, each multimer
10 comprising at least two monomer domains, immuno domains or combinations thereof;
11 screening the library of multimers for the ability to bind to the first target
12 molecule; and
13 identifying a multimer that binds to the first target molecule.

1 38. The method of claim 37, wherein the monomer domains each bind an
2 ion.

1 39. The method of claim 38, wherein the ion is selected from the group
2 consisting of calcium and zinc.

1 40. The method of claim 37, wherein the monomer domains are selected
2 from the group consisting of an A domain, EGF domain, EF Hand, Cadherin domain, C-type
3 lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and zinc finger.

1 41. A library of multimers, wherein
2 each multimer comprises at least two monomer domains connected by a
3 linker; and
4 each monomer domain binds an ion.

1 42.. The library of claim 41, wherein the ion is selected from calcium and
2 zinc.

1 43. The library of claim 41, wherein each monomer domain of the
2 multimers is a non-naturally occurring monomer domain.

1 44. The library of claim 41, wherein the monomer domains are between 25
2 and 500 amino acids.

1 45. The library of claim 41, wherein the polypeptide domains are selected
2 from the group consisting of consisting of an A domain, EGF domain, EF Hand, Cadherin
3 domain, C-type lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and
4 zinc finger.

1 46. The library of claim 41, wherein the monomer domain is an LDL
2 receptor class A domain monomer comprising the following sequence:

3 $C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$

4 wherein C is cysteine, X_{n-m} represents between n and m number of
5 independently selected amino acids, and (D,N) indicates that the position can be either D or
6 N; and

7 wherein C_a-C_e , C_b-C_e and C_d-C_f form disulfide bonds.

1 47. The library of claim 46, wherein the monomer domain is an LDL
2 receptor class A domain monomer comprising the following sequence:

3 $CaX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$

4 wherein X is defined as follows:

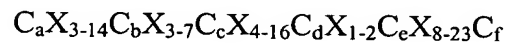
X(6,7)							X(4,5)				X(6)						X(5)					X(8,10)									
X1	X2	X3	X4	X5	X6		X1	X2	X3	X4		X1	X2	X3	X4	X5	X6	X1	X2	X3	X4	X5	X1	X2	X3	X4	X5	X6	X7	X8	
A	A	A	A	A	A		A	A		A	C	A	A	A	A	A		A	A		A		A	A	A	A	A	A	A	A	
D	D	D	D				D	D	D	D	D	D	D	D	D	D		D	D	D	D	D	D	D	D	D	D	D	D	D	
E	E	E	E	E	F		E	D	E	F	E	E	E	E	E	E		E	E	E	E	E	E	E	E	E	E	E	E	E	
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G	G	G	G	G	H		G	H	H	H	G	G	G	G	G	G		G	G	G	G	G	G	G	G	G	G	G	G	G	
H	H	H	H	H	I		H	I	I	I	H	I	I	I	I	I		H	H	H	H	H	H	H	H	H	H	H	H	H	
I	I	I	I	I	K		K	K	K	K	K	K	K	K	K	K		K	K	K	K	K	K	K	K	K	K	K	K	K	
K	K	K	K	K	L		L	L	L	L	L	L	L	L	L	L		L	L	L	L	L	L	L	L	L	L	L	L	L	
L	L	L	L	L	M		M	M	M	M	M	M	M	M	M	M		M	M	M	M	M	M	M	M	M	M	M	M	M	
M	M	M	M	M	N		N	N	N	N	N	N	N	N	N	N		N	N	N	N	N	N	N	N	N	N	N	N	N	
N	N	N	N	N	P		P	Q	Q	Q	Q	Q	Q	Q	Q	Q		Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	
P	P	P	P	P	Q		Q	R	R	R	R	R	R	R	R	R		R	R	R	R	R	R	R	R	R	R	R	R	R	
Q	Q	Q	Q	Q	R		R	S	S	S	S	S	S	S	S	S		S	S	S	S	S	S	S	S	S	S	S	S	S	
R	R	R	R	R	S		S	T	T	T	T	T	T	T	T	T		T	T	T	T	T	T	T	T	T	T	T	T	T	
S	S	S	S	S	T		T	V	V	V	V	V	V	V	V	V		V	V	V	V	V	V	V	V	V	V	V	V	V	
T	T	T	T	T	V		V	W	W	W	W	W	W	W	W	W		W	W	W	W	W	W	W	W	W	W	W	W	W	
V	V	V	V	V	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
Y	Y	Y	Y	Y																											

X1	X2	X3	X4	X5	X6	X7
A	A					A
D	D	D	D	D		
E	E	E	E	E	F	E
F	F	F	F	F		G
G	G	G	G	G		H
H						
K	L	L	K	K	L	K
L	L	L	L	L	L	L
M						
N	N	N	N	N	N	N
P	P	P	P	P	P	P
Q	Q	Q	Q	Q	Q	Q
R	R	R	R	R	R	R
S	S	S	S	S	S	S
T	T	T	T	T	T	T
V	V	V	V	V	V	V
W						
Y	Y	Y	Y	Y	Y	Y

X1	X2	X3	X4	X5	X6	X7	X8	X9
A	A					A	A	A
D	D			D			D	D
E	E				E	E	E	E
F	G							
G		G				G	G	
H		H				H		H
I								
K								
L	L					L		L
M						M	N	N
N	N					N	P	P
P						P	Q	Q
Q	Q					Q	R	R
R						R	S	S
S	S					S		
T	T					T		
V							V	
W								
Y	Y	Y	Y	Y	Y	Y	Y	Y

X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
						A	A	A	A
D	D			D		D	D	D	D
E	E	E	E	E	E	E	E	E	E
F	F								
G	G	H				G		G	H
H	H					H	H	H	I
I	I					I	I	I	I
K	K	L				K	K	K	L
L						L	L	L	L
M						M	M	M	M
N	N					N	N	N	N
P						P	P	P	P
Q	Q					Q	Q	Q	Q
R	R	S				R	R	R	R
S	S	S	T			S	S	S	T
	W					W			
Y							Y	Y	Y

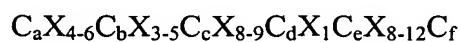
48. The library of claim 41, wherein the monomer domain is an EGF domain monomer comprising the following sequence:



wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids; and

wherein C_a - C_c , C_b - C_e and C_d - C_f form disulfide bonds.

49. The library of claim 48, wherein the monomer domain is an EGF domain monomer comprising the following sequence:



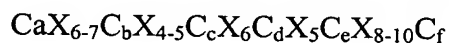
wherein X is defined as follows:

C	X(4,6)				C	X(3,5)			C	X(8,9)								C	X(1)	C	X(8/12)												C
X1 X2 X3 X4					X1 X2 X3			X1 X2 X3 X4 X5 X6 X7 X8								X1	X1 X2 X3 X4 X5 X6 X7 X8																
A A A A					A A			A A A A A A A A								A	A A A A A A A A																
D D D					D D			D D D D D D D								D	D D D D D D D																
E E E E					E F F			E E E E E E E								E	E E E E E E E																
F G G G					F G H I			F F F F F F F								F	F F F F F F F																
G H H H					G H H I			G H H I H I H								H	H H H H H H H																
I K K K					I K L			I K K K K L L								I	I K K K K L L																
L L L L					L L			L L L L L L L								L	L L L L L L L																
M L M N					M N N			M L M N M N								M	M L M N M N																
N N N P					N N N			N N N P P P P								N	N N N P P P P																
P P P Q					P Q Q			P Q Q R R R R								P	P Q Q R R R R																
Q R R S					Q R S T			Q R R S T T V								Q	Q R R S T T V																
R S T T					R S T V			R S T T V V W								R	R S T T V V W																
S T V W					S T V			S T T V V Y								S	S T T V V Y																
T V W Y					T V Y			T V V Y Y Y								T	T V V Y Y Y																
V W Y Y					V Y Y			V W W Y Y Y								V	V W W Y Y Y																
W Y Y Y					W Y Y			W Y Y Y Y Y								W	W Y Y Y Y Y																
Y Y Y Y					Y Y			Y Y Y Y Y Y								Y	Y Y Y Y Y Y																
X1 X2 X3 X4 X5					X1 X2 X3 X4			X1 X2 X3 X4 X5 X6 X7 X8 X9									X1 X2 X3 X4 X5 X6 X7 X8 X9 X10 X11 X12																
A A A A A					A A A A			A A A A A A A A									A A A A A A A A																
D D D D					D D D			D D D D D D D									D D D D D D D																
E E E E F					E E E			E E E E E E E									E E E E E E E																
F F F F G					F F F G			F F F G G G									F F F G G G																
G G G H					G H I K			G G G H H H									G G G H H H																
H H H I					H I K L			H H H L L L									H H H I K L																
I K L L					I K L M			I K L M N N									I K L M N N																
L L L M					L L M N			L L M N P P									L L M N P P																
M L M N					M N P Q			M N P Q R R									M N P Q R R																
N N N P					N P Q R			N P Q R S T									N P Q R S T																
P P P Q					P Q R S			P Q R S T V									P Q R S T V																
Q R R S					Q R S T			Q R S T V W									Q R S T V W																
R R S T					R S T V			R S T V W Y									R S T V W Y																
S T T V					S T V			S T V W Y Y									S T V W Y Y																
T V W Y					T V Y			T V Y Y Y Y									T V Y Y Y Y																
V W Y Y					V Y			V W Y Y Y Y									V W Y Y Y Y																
W Y Y Y					W Y Y			W Y Y Y Y Y									W Y Y Y Y Y																
Y Y Y Y					Y Y Y			Y Y Y Y Y Y									Y Y Y Y Y Y																
X1 X2 X3 X4 X5 X6					X1 X2 X3 X4 X5			X1 X2 X3 X4 X5 X6 X7 X8																									
A A A A A A					A A A A A			A A A A A A A																									
D D D D D					D D D D			D D D D D D D																									
E E E E E					E E E E			E E E E E E E																									
F F F F F					F F F F			F F F F F F F																									
G G G G G					G G G G			G G G G G G G																									
H H H H I					H H H H			H H H H H H H																									
I K K K K					I K K K			I K K K K K K																									
L L L L L					L L L L			L L L L L L L																									
M L M N					M L M N			M L M N M N																									
N N N P					N N N			N N N P Q R																									
P P P Q					P P Q R			P P Q R S T																									
Q R R S					Q R S T			Q R S T V W																									
R R S T					R S T V			R S T V W Y																									
S T T V					S T V			S T V W Y Y																									
T V W Y					T V Y			T V Y Y Y Y																									
V W Y Y					V Y Y			V W Y Y Y Y																									
W Y Y Y					W Y Y			W Y Y Y Y Y																									
Y Y Y Y					Y Y Y			Y Y Y Y Y Y																									

50. The library of claim 41, wherein the monomer domains are linked by a polypeptide linker.

- 1 51. The library of claim 50, wherein the linker is between 1-20 amino acid
2 residues.
- 1 52. The library of claim 50, wherein the polypeptide linker is naturally
2 associated with the monomer domain.
- 1 53. The library of claim 41, wherein the monomer domains form a
2 secondary structure by the formation of disulfide bonds.
- 1 54. The library of claim 53, wherein the multimers comprise an A domain
2 connected to a monomer domain by a polypeptide linker.
- 1 55. The library of claim 54, wherein the linker comprises the following
2 sequence, $A_1A_2A_3A_4A_5A_6$, wherein
3 A_1 is selected from the amino acids A, P, T, Q, E and K;
4 A_2 and A_3 are any amino acid except C, F, Y, W, or M;
5 A_4 is selected from the amino acids S, G and R;
6 A_5 is selected from the amino acids H, P, and R
7 A_6 is the amino acid, T.
- 1 56. A polypeptide comprising at least two monomer domains separated by
2 a heterologous linker, wherein each monomer domain specifically binds to a target molecule
3 and each monomer domain binds an ion.
- 1 57. The polypeptide of claim 56, wherein the ion is selected from calcium
2 and zinc.
- 1 58. The polypeptide of claim 56, wherein the monomer domain is an LDL
2 receptor class A domain monomer comprising the following sequence:
3 $C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$
4 wherein C is cysteine, X_{n-m} represents between n and m number of
5 independently selected amino acids, and (D,N) indicates that the position can be either D or
6 N; and
7 wherein C_a-C_c , C_b-C_e and C_d-C_f form disulfide bonds.

59. The polypeptide of claim 58, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:



wherein X is defined as follows:

C	X(6,7)						C	X(4,5)				C	X(6)						C	X(5)					C	X(8,10)								C
X1	X2	X3	X4	X5	X6		X1	X2	X3	X4		X1	X2	X3	X4	X5	X6	X1	X2	X3	X4	X5		X1	X2	X3	X4	X5	X6	X7	X8			
A	A	A	A	A	A		A	A			A	C	D	E	F	G	H	A	A	A			A	A	A				A	A				
D	E	D	D	E		E	D	D	E	D	E	D	E	D	E	E		D	D	D		D	E	D	D	D	D	D	D	D				
F	G	F	F	F	F	F	F	G	F	F	F	F	F	F	F			E	F	F	F	F	F	F	F	F	F	F	F	F				
G	H	G	H	G	H	H	H	H	H	H	H	H	H	H	H			H	H	G	H	H	H	H	H	H	H	H	H	H				
K	K	K	K	K	K	K	K	K	K	K	K	K	K	K	K			K	K	K	K	K	K	K	K	K	K	K	K	K				
L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L			L	L	L	L	L	L	L	L	L	L	L	L	L				
M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M			M	M	M	M	M	M	M	M	M	M	M	M	M				
N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N			N	N	N	N	N	N	N	N	N	N	N	N	N	N			
P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P			P	P	P	P	P	P	P	P	P	P	P	P	P				
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q			Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q				
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R			R	R	R	R	R	R	R	R	R	R	R	R	R	R			
S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S			S	S	S	S	S	S	S	S	S	S	S	S	S	S			
T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T			T	T	T	T	T	T	T	T	T	T	T	T	T	T			
V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V			V	V	V	V	V	V	V	V	V	V	V	V	V	V			
W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W			W	W	W	W	W	W	W	W	W	W	W	W	W	W			
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y			Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y			

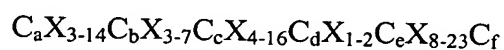
X1	X2	X3	X4	X5	X6	X7
A	A					A
D	E	D	D	E		E
F	E	F	F	F	F	
G	G	G	G	G		G
H	H		H			H
K		K	K	K	K	K
L	L	L		L	L	L
M		M				M
N	N	N	N	N	N	
P	P	P	P	P	P	
Q	Q	Q	Q	Q	Q	
R	R	R	R	R	R	
S	S	S	S	S	S	
T	T	T	T	T	T	
V	V	V	V	V	V	
W	W	W	W	W	W	
Y	Y	Y	Y	Y	Y	Y

X1	X2	X3	X4	X5
A	A	A	A	A
D	E	D	E	D
F	G	F	G	F
H	H	H	H	H
K	K	K	K	K
L	L	L	L	L
M	M	M	M	M
N	N	N	N	N
P	P	P	P	P
Q	Q	Q	Q	Q
R	R	R	R	R
S	S	S	S	S
T	T	T	T	T
V	V	V	V	V
W	W	W	W	W
Y	Y	Y	Y	Y

X1	X2	X3	X4	X5	X6	X7	X8	X9
A	A					A	A	A
D	D			D			D	D
E	E			E	E	E	E	E
F	F			F			F	F
G	G			G			G	G
H	H			H			H	H
K	K			K			K	K
L	L			L			L	L
M	M			M			M	M
N	N			N			N	N
P	P			P			P	P
Q	Q			Q			Q	Q
R	R			R			R	R
S	S			S			S	S
T	T			T			T	T
V	V			V			V	V
W	W			W			W	W
Y	Y			Y			Y	Y

X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
A	A	A	A	A	A	A	A	A	A
D	D		D		D	D	D	D	D
E	E		E		E	E	E	E	E
F	F		F		F	F	F	F	F
G	G		G		G	G	G	G	G
H	H		H		H	H	H	H	H
K	K		K		K	K	K	K	K
L	L		L		L	L	L	L	L
M	M		M		M	M	M	M	M
N	N		N		N	N	N	N	N
P	P		P		P	P	P	P	P
Q	Q		Q		Q	Q	Q	Q	Q
R	R		R		R	R	R	R	R
S	S		S		S	S	S	S	S
T	T		T		T	T	T	T	T
V	V		V		V	V	V	V	V
W	W		W		W	W	W	W	W
Y	Y		Y		Y	Y	Y	Y	Y

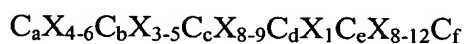
60. The polypeptide of claim 56, wherein the monomer domain is an EGF domain monomer comprising the following sequence:



wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids; and

wherein C_a-C_c , C_b-C_e and C_d-C_f form disulfide bonds.

61. The polypeptide of claim 60, wherein the monomer domain is an EGF domain monomer comprising the following sequence:



wherein X is defined as follows:

C X(4,6)				C X(3,5)			C X(8,9)								C X(1) C		X(8/12)								C		
X1	X2	X3	X4	X1	X2	X3	X1	X2	X3	X4	X5	X6	X7	X8	X1	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11	X12
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	
D	D	D	E	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	
E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	
F	F	F	G	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	
G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	
H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	
I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	
K	K	K	L	K	L	L	K	L	L	L	L	L	L	L	K	L	L	L	L	L	L	L	L	L	L	L	
L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	
M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	
S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	
V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	
W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	

X1	X2	X3	X4	X5	X1	X2	X3	X4	X1	X2	X3	X4	X5	X6	X7	X8	X9
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D	D
E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E
F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G
H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
K	K	K	L	L	K	L	L	L	K	L	L	L	L	L	L	L	L
L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L
M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T
V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V
W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

X1	X2	X3	X4	X5	X6	X7	X8
A	A	A	A	A	A	A	A
D	D	D	D	D	D	D	D
E	E	E	E	E	E	E	E
F	F	F	F	F	F	F	F
G	G	G	G	G	G	G	G
H	H	H	H	H	H	H	H
I	I	I	I	I	I	I	I
K	K	L	L	L	L	L	L
L	L	L	L	L	L	L	L
M	M	M	M	M	M	M	M
N	N	N	N	N	N	N	N
P	P	P	P	P	P	P	P
Q	Q	Q	Q	Q	Q	Q	Q
R	R	R	R	R	R	R	R
S	S	S	S	S	S	S	S
T	T	T	T	T	T	T	T
V	V	V	V	V	V	V	V
W	W	W	W	W	W	W	W
Y	Y	Y	Y	Y	Y	Y	Y

X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11	X12
A	A	A	A	A	A	A	A	A	A	A	A
D	D	D	D	D	D	D	D	D	D	D	D
E	E	E	E	E	E	E	E	E	E	E	E
F	F	F	F	F	F	F	F	F	F	F	F
G	G	G	G	G	G	G	G	G	G	G	G
H	H	H	H	H	H	H	H	H	H	H	H
I	I	I	I	I	I	I	I	I	I	I	I
K	K	L	L	L	L	L	L	L	L	L	L
L	L	L	L	L	L	L	L	L	L	L	L
M	M	M	M	M	M	M	M	M	M	M	M
N	N	N	N	N	N	N	N	N	N	N	N
P	P	P	P	P	P	P	P	P	P	P	P
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q
R	R	R	R	R	R	R	R	R	R	R	R
S	S	S	S	S	S	S	S	S	S	S	S
T	T	T	T	T	T	T	T	T	T	T	T
V	V	V	V	V	V	V	V	V	V	V	V
W	W	W	W	W	W	W	W	W	W	W	W
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

X1	X2	X3	X4	X5
A	A	A	A	A
D	D	D	D	D
E	E	E	E	E
F	F	F	F	F
G	G	G	G	G
H	H	H	H	H
I	I	I	I	I
K	K	L	L	L
L	L	L	L	L
M	M	M	M	M
N	N	N	N	N
P	P	P	P	P
Q	Q	Q	Q	Q
R	R	R	R	R
S	S	S	S	S
T	T	T	T	T
V	V	V	V	V
W	W	W	W	W
Y	Y	Y	Y	Y

1 62. The polypeptide of claim 56, wherein each monomer domain is a non-
2 naturally occurring protein monomer domain.

1 63. The polypeptide of claim 56, wherein the polypeptide comprises a first
2 monomer domain that binds a first target molecule and a second monomer domain that binds
3 a second target molecule.

1 64. The polypeptide of claim 56, wherein the polypeptide comprises two
2 monomer domains, each monomer domain having a binding specificity for a different site on
3 a first target molecule.

1 65. The polypeptide of claim 56, wherein the monomer domains are
2 between 25 and 500 amino acids.

1 66. The polypeptide of claim 56, wherein the polypeptide comprises at
2 least three monomer domains.

1 67. The polypeptide of claim 56, wherein the polypeptide comprises four
2 monomer domains.

1 68. The polypeptide of claim 56, comprising polypeptide has an improved
2 avidity for a target molecule compared to the avidity of a monomer domain alone.

1 69. The polypeptide of claim 68, wherein the avidity of the polypeptide is
2 at least two times the avidity of a monomer domain alone.

1 70. The polypeptide of claim 56, wherein the monomer domain is selected
2 from the group consisting of an A domain, EGF domain, EF Hand, Cadherin domain, C-type
3 lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and zinc finger.

1 71. The polypeptide of claim 56, wherein the target molecule is selected
2 from the group consisting of a viral antigen, a bacterial antigen, a fungal antigen, an enzyme,
3 a cell surface protein, an enzyme inhibitor, a reporter molecule, and a receptor.

1 72. The polypeptide of claim 73, wherein the domains form a secondary
2 structure by the formation of disulfide bonds.

1 73. The polypeptide of claim 56, wherein the monomer domains are linked
2 by a polypeptide linker.

1 74. The polypeptide of claim 73, wherein the polypeptide linker is a
2 naturally-occurring linker associated with the monomer domain.

1 75. The polypeptide of claim 73, wherein the linker is between 1-20 amino
2 acids.

1 76. The polypeptide of claim 73, wherein the linker comprises the
2 following sequence, $A_1A_2A_3A_4A_5A_6$, wherein

3 A_1 is selected from the amino acids A, P, T, Q, E and K;

4 A_2 and A_3 are any amino acid except C, F, Y, W, or M;

5 A_4 is selected from the amino acids S, G and R;

6 A_5 is selected from the amino acids H, P, and R

7 A_6 is the amino acid, T.

1 77. A method for identifying a human chimeric monomer domain that
2 binds to a target molecule, said method comprising:

3 providing a sequence alignment of at least two naturally occurring human
4 monomer domains from the same family of monomer domains;

5 identifying amino acid residues in corresponding positions in the human
6 monomer domain sequences that differ between the human monomer domains;

7 generating a library of human chimeric monomer domains, wherein each
8 human chimeric monomer domain sequence consists of amino acid residues that correspond
9 in type and position to residues from two or more naturally occurring human monomer
10 domains from the same family of monomer domains;

11 screening the library of human chimeric monomer domains for binding to a
12 target molecule; and

13 identifying a human chimeric monomer domain that binds to a target
14 molecule.

1 78. The method of claim 77 wherein the naturally occurring human
2 monomer domains are LDL receptor A-domain monomers.

1 79. The method of claim 77 wherein the naturally occurring human
2 monomer domains are EGF-like domain monomers.

1 80. The method of claim 77 wherein the screening of the library is carried
2 out using a two-hybrid screening method.

1 81. A method of producing a polypeptide comprising the multimer
2 identified in claim 77.

1 82. The method of claim 82, wherein the polypeptide is produced by
2 recombinant gene expression.

1 83. A non-naturally-occurring polypeptide comprising an LDL receptor
2 class A domain monomer, wherein the monomer comprises the following sequence:

3 $C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$

4 wherein C is cysteine, X_{n-m} represents between n and m number of
5 independently selected amino acids, and (D,N) indicates that the position can be either D or
6 N; and

7 wherein C_a-C_c , C_b-C_e and C_d-C_f form disulfide bonds.

1 84. The polypeptide of claim 83, wherein the monomer domain is an LDL
2 receptor class A domain monomer comprising the following sequence:

3 $CaX_{6-7}CbX_{4-5}CcX_6CdX_5CeX_{8-10}Cf$

4 wherein X is defined as follows:

X(6,7)							X(4,5)				X(6)						X(5)					X(8,10)							
X1	X2	X3	X4	X5	X6		X1	X2	X3	X4	X1	X2	X3	X4	X5	X6	X1	X2	X3	X4	X5	X1	X2	X3	X4	X5	X6	X7	X8
A	A	A	A	A	A		A	A		A	A	A	A	A	A		A	A	A			A	A	A	A	A	A	A	
C																													
D	D	D					D	D	D		D	D	D	D			D	D	D	D		D	D	D	D	D	D	D	D
E	E	E	E			E	E	E	E		E	E	E	E			E	E	E	E		E	E	E	E	E	E	E	E
F	F	F	F		F		F	F	F	F	F	F	F	F			F	F	F	F		F	F	F	F	F	F	F	F
G	G	G	G				G	G	G	G	G	G	G	G			G	G	G	G		G	G	G	G	G	G	G	G
H	H	H	H		H	H	H	H	H		H	H	H	H			H	H	H	H		H	H	H	H	H	H	H	H
I	I						I				I	I	I	I			I	I	I	I		I	I	I	I	I	I	I	I
K	K	K	K	K	K	L	K		K	K	K	K	K	K	L		K	K	K	K		K	K	K	K	K	K	K	K
L	L	L	L	L	L	L	L		L	L	L	L	L	L	L		L	L	L	L		L	L	L	L	L	L	L	L
M	M					M					M	M	M	M	M		M	M	M	M		M	M	M	M	M	M	M	M
N	N	N	N	N		N	N	N	N		N	N	N	N	N		N	N	N	N		N	N	N	N	N	N	N	N
P	P	P	P			P	P				P	P	P	P	P		P	P	P	P		P	P	P	P	P	P	P	P
Q	Q	Q	Q	Q	Q		Q	Q	Q	Q	Q	Q	Q	Q	Q		Q	Q	Q	Q		Q	Q	Q	Q	Q	Q	Q	Q
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R		R	R	R	R		R	R	R	R	R	R	R	R
S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S		S	S	S	S		S	S	S	S	S	S	S	S
T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T		T	T	T	T		T	T	T	T	T	T	T	T
V	V	V				V	V				V	V	V	V	V		V	V	V	V		V	V	V	V	V	V	V	V
W	W	W				W					W	W	W	W	W		W	W	W	W		W	W	W	W	W	W	W	W
Y	Y	Y	Y			Y	Y				Y	Y	Y	Y	Y		Y	Y	Y	Y		Y	Y	Y	Y	Y	Y	Y	Y

X1	X2	X3	X4	X5	X6	X7		X1	X2	X3	X4	X5		X1	X2	X3	X4	X5	X6	X7	X8	X9
A	A					A		A	A	A	A			A	A					A	A	A
D	D	D	D	D				D	D	D	D	D		D	D					D	D	D
E	E	E		E	E		E	E	E	E	E			E	E	E	E			E	E	E
F	F	F	F			F		F						F								
G	G	G	G	G		G		G	G	G	G			G						G	G	G
H	H			H		H		H	H	H	H			H						H	H	H
K		K	K	K		K		K	K	K	K	L		K						K	K	K
L	L	L		L		L		L				M		L						L	L	L
M				M										M						M	M	M
N	N	N	N	N		N		N	N	N	N			N						N	N	N
P	P	P	P			P		P	P	P	P	Q		P						P	P	P
Q	Q	Q	Q	Q	Q		Q	Q	Q	Q	Q	R		Q						Q	Q	Q
R	R	R	R	R	R	R		R	R	R	R	S		R						R	R	R
S	S	S	S	S	S	S		S	S	S	S	T		S						S	S	S
T	T	T	T	T	T	T		T	T	T	T	V		T						T	T	T
V	V	V	V	V	V	V		V	V	V	V	W		V						V	V	V
W						W								W								
Y						Y								Y						Y	Y	Y

X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
A						A	A	A	A
D	D			D		D	D	D	D
E		F		E		E	E	E	E
G		G	H			G		H	H
K	K						K	K	K
L		L					L	M	L
N	N						N	N	N
P							P	P	P
Q	Q	Q	S				Q	Q	Q
R	R	R					R	R	R
S	S	S	T				S	S	S
W							W		
Y							Y	Y	Y

- 5
- 1 85. The polypeptide of claim 83, wherein the polypeptide is 65 or fewer
- 2 amino acids long.
- 1 86. The polypeptide of claim 83, wherein the monomer is fused to a
- 2 heterologous amino acid sequence.
- 1 87. The polypeptide of claim 83, wherein the monomer binds to a target
- 2 molecule.

1 88. The polypeptide of claim 86, wherein the heterologous amino acid
2 sequence is selected from an affinity peptide, a heterologous LDL receptor class A domain, a
3 heterologous EGF domain, a purification tag, an enzyme, and a reporter protein.

1 89. A non-naturally-occurring polypeptide comprising an EGF domain
2 monomer, wherein the EGF domain monomer comprises the following sequence:

3 $C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$

4 wherein C is cysteine, X_{n-m} represents between n and m number of
5 independently selected amino acids; and

6 wherein C_a-C_c , C_b-C_e and C_d-C_f form disulfide bonds.

1 90. The polypeptide of claim 89, wherein the monomer domain is an EGF
2 domain monomer comprising the following sequence:

3 $C_aX_{4-6}C_bX_{3-5}C_cX_{8-9}C_dX_1C_eX_{8-12}C_f$

4 wherein X is defined as follows:

X(4,6)				X(3,5)			X(8,9)								X(8,12)							
X1	X2	X3	X4	X1	X2	X3	X1	X2	X3	X4	X5	X6	X7	X8	X1	X2	X3	X4	X5	X6	X7	X8
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
D	D	D		D		D	D	D	D	D		D		D	D	D	D	D	D	D	D	D
E	E	E	E	E		E	E	E	E	E		E		E	E	E	E	E	E	E	E	E
F					F	F	F	F	F	F		F		F	F	F	F	F	F	F	F	F
G	G	G	G		G	G	G	G	G	G		G		G	G	G	G	G	G	G	G	G
H	H	H		H	H	H	H	H	H	H		H		H	H	H	H	H	H	H	H	H
I															I	I	I	I	I	I	I	I
K	K	K		K		K	K	K	K	K		K		K	K	K	K	K	K	K	K	K
L	L	L		L		L	L	L	L	L		L		L	L	L	L	L	L	L	L	L
M			M				M	M	M	M		M		M	M	M	M	M	M	M	M	M
N	N	N	N	N	N	N	N	N	N	N		N		N	N	N	N	N	N	N	N	N
P	P	P	P	P	P	P	P	P	P	P		P		P	P	P	P	P	P	P	P	P
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q		Q		Q	Q	Q	Q	Q	Q	Q	Q	Q
R	R	R	R	R	R	R	R	R	R	R		R		R	R	R	R	R	R	R	R	R
S	S	S	S	S	S	S	S	S	S	S		S		S	S	S	S	S	S	S	S	S
T	T	T	T	T	T	T	T	T	T	T		T		T	T	T	T	T	T	T	T	T
V				V		V	V	V	V	V		V		V	V	V	V	V	V	V	V	V
W			W				W	W	W	W		W		W	W	W	W	W	W	W	W	W
Y	Y			Y		Y	Y	Y	Y	Y		Y		Y	Y	Y	Y	Y	Y	Y	Y	Y

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- 1

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91. The polypeptide of claim 89, wherein the EGF domain monomer is fused to a heterologous amino acid sequence.
- 1

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92. The polypeptide of claim 89, wherein the monomer binds to a target molecule.
- 1

2

93. The polypeptide of claim 89, wherein the polypeptide is 45 or fewer amino acids long.

1 94. The polypeptide of claim 91, wherein the heterologous amino acid
2 sequence is selected from an affinity peptide), a heterologous LDL receptor class A domain, a
3 heterologous EGF domain, a purification tag, an enzyme, and a reporter protein.